Alerts, Notices, and Case Reports

Mushroom Poisoning due to Amatoxin

Northern California, Winter 1996–1997

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OF MORE THAN 5,000 SPECIES of mushrooms in the United States, approximately 100 are poisonous, and less than a dozen are deadly.[1–3] More than 90% of deaths are attributable to *Amanita phalloides*, (*A. phalloides*) also referred to as the "death cap."[3–5] Ingestion of a single *A. phalloides* mushroom can be lethal.[2,6]

A. phalloides poisonings have increased in the United States and California.[7,8] In California during the winter of 1995–1996, 13 people were hospitalized after eating *A. phalloides*[8]; 10 poisonings due to *A. phalloides* occurred between 27 December 1996 and 5 January 1997 in Northern California; 2 patients died. Our investigation describes these 10 patients; we offer suggestions for clinicians and recommendations for preventing future cases.

Report of Cases

In early January 1997, the California Department of Health Services was notified by a liver transplant unit at a tertiary care hospital about an apparent cluster of mushroom poisonings. We sought additional cases by contacting local health departments and the California Poison Control System. A case-patient was defined as a person with vomiting and diarrhea beginning ≥6 hours after consuming wild mushrooms in California during December 1996 or January 1997.

In addition to reviewing the medical records of all 10 case-patients, we interviewed 7 of the 8 survivors directly and a relative of each of the 2 deceased patients. We asked about prior illness after eating wild mushrooms and their awareness of the risk of wild mushroom poisoning. We queried case-patients where they collected mushrooms and their knowledge and prior experience in collecting mushrooms.

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Results

Demographics and Clinical Information

Nine of the 10 case-patients were men; the median age was 23 years (range 12–68 years). Of 9 with race/ethnicity information, 6 were white/non-Hispanic, 2 were Filipino, and 1 was multiracial (white/African-American). Patients resided in Alameda, Mendocino, San Francisco, Santa Clara, and Sonoma counties in California.

The median interval from ingestion to the onset of gastrointestinal symptoms was 12 hours (range 8–26 hours). Reported symptoms included vomiting (100% of patients), diarrhea (100%), nausea (100%), abdominal cramping (60%), and weakness (70%). Nine patients were hospitalized for a median of 6 days (range 2–8 days); the two deaths occurred on the sixth and eighth hospital days. Serum transaminases peaked 2 to 4 days after mushroom consumption; the median peak aspartate aminotransferase (AST) was 3,284 U/liter (range 594–6,998 U/liter; normal range 0–35 U/liter), and the median peak alanine aminotransferase (ALT) was 4,660 U/liter (range 38–7,120 U/liter; normal range 0–35 U/liter).[9] For the eight patients with prothrombin time (PT) results, the median PT was 18.0 sec (range 12.7 to >60 sec, normal range 11–15 sec) (Table 1).[9]

Treatment included intravenous hydration (100% of patients), H_2-blockers (100%), activated charcoal (90%), penicillin (60%), and *N*-acetylcysteine (80%). Fresh frozen plasma and vitamin K were administered to 30% and 60% of patients, respectively. Six patients received repeated doses of activated charcoal. Five of the 9 hospitalized patients were transferred to a tertiary-care hospital; none had liver transplantation; 2 died before liver transplant could be arranged. The 2 fatal case-patients had multiorgan failure; both required hemodialysis, and 1 required ventilatory support. The two deaths occurred in patients with the highest PTs.

Knowledge and awareness of the dangers of mushroom collection and ingestion

Of the three mushroom collectors interviewed, all believed they could identify poisonous mushrooms. No mushrooms had been presented to and examined by an expert mycologist before ingestion. Two collectors incorrectly thought that poisonous mushrooms could be identified by color. One incorrectly thought the presence of a "cup" or volva at the base of the stem indicated that the mushroom was edible (a volva is actually a feature of

TABLE 1.—*Case-Patient Information, Mushroom Poisoning, California, 1996–1997*

Patient	Age	Sex	Outcome	Hospital Days	Peak AST (U/liter)	Peak ALT (U/liter)	Peak PT (sec)	Latency Period to Gastrointestinal Symptoms (hours)	Time to Medical Care (hours)	Time to Diagnosis (hours)
Group 1										
1	42	M	Recovery	6	3,284	6,000	32.1	12	16.5	16.5
2	17	M	Recovery	6	2,378	4,639	12.7	15	17.5	17.5
3	12	M	Recovery	6	2,162	4,808	31.7	16	17.5	17.5
Group 2										
4	18	M	Recovery	3	6,998	5,794	15.8	13	43	43
5	19	M	Recovery	2	594	930	NA	11	48	48
6	17	M	Recovery	0	19	38	NA	11	46	46
Group 3										
7	30	M	Recovery	4	2,392	3,062	18.0	12	25	25
8	28	F	Recovery	3	3,632	7,120	17.7	12	12–24	39
Group 4										
9	32	M	Death	8	4,276	4,313	60.0	8	21	21
Group 5										
10	68	M	Death	6	3,499	4,681	34.0	12	27	~120

Amanita species). Other erroneous methods mentioned by these collectors included the avoidance of bitter-tasting mushrooms and mushrooms with a milky discharge when cut.

Case-patients did not report illness after eating wild mushrooms in the past, yet they all knew that some mushrooms are poisonous. Only one had heard about mushroom poisoning from the media during the year before his mushroom poisoning. Three patients were unaware that they had actually eaten wild mushrooms, since the poisonous mushrooms were an ingredient in foods prepared by others. None of the interviewed patients planned to eat wild mushrooms in the future.

Case Circumstances

The first group was a Russian family; the parents collected wild mushrooms while hiking near Lake Chabot in the San Francisco Bay Area. This was the first time that the father had collected mushrooms in the United States after moving from Russia 2 years earlier. He collected mushrooms with impunity in Russia for approximately 30 years and thought that he knew the types of mushrooms that he was collecting. He had learned about collecting mushrooms from family members with years of mushroom collecting experience, from books and field guides, and from a botany class in a Russian middle school.

The mushrooms were fried and eaten by the father and his two sons, who became ill 12 to 16 hours after eating the mushrooms. All three ill family members were diagnosed at a local emergency department, transferred to a tertiary care facility, and discharged 6 days later (Table 1). Fragments of one variety of the leftover mushrooms were identified as *Boletus amygdalinus*, which is limited in toxicity to gastrointestinal symptoms.

In the second group, an 18-year-old white man collected mushrooms after hiking about 0.4 km (0.25 miles) from a road in rural Mendocino county. He had collected mushrooms 8 to 10 times previously and thought these mushrooms were "caesars." (He may have been referring to *A. caesarea*, an edible mushroom, which looks much like *A. phalloides*. Even experts may have a difficult time distinguishing the two.) He had learned about mushroom collecting from books, field guides, and a friend with more than 15 years of collecting experience.

The mushrooms were dried, prepared with deviled eggs, and served at a small New Year's Eve party. He and two friends ate the mushrooms at the party. The collector was evaluated in the emergency department of a local medical center and transferred to a tertiary-care facility. The two friends were then contacted by the local medical center for evaluation. One friend was hospitalized; the other was followed as an outpatient. The two hospitalized patients improved and were discharged after 2 to 3 days (Table 1). Leftovèr mushrooms were identified as *A. phalloides*.

In the third group, a 30-year-old Filipino man collected mushrooms after hiking about 1.2 km (0.75 miles) at a local regional park in Oakland. He had collected wild mushrooms twice in the previous 4 years but had not previously noticed this variety of mushroom. He learned about mushrooms by reading books and field guides. He prepared the mushrooms in a soup for himself and a girlfriend, became ill, and was hospitalized about 25 hours later. His girlfriend was initially diagnosed with ulcer/dyspepsia and prescribed cimetidine at a medical clinic. Because of her continued nausea, vomiting, and diarrhea, she sought medical care in an emergency department where the history of wild mushroom ingestion was obtained, and she was hospitalized approximately 39 hours after eating the wild mushrooms. Both patients improved and were discharged after 3 to 4 days (Table 1). No mushrooms were available for identification.

In the fourth "group," a 32-year-old white man collected mushrooms in his girlfriend's backyard. As a child, he learned about mushroom collecting from relatives who had collected mushrooms for many years in Italy. He sautéed the mushrooms in butter. He was diagnosed with mushroom poisoning in the emergency department of a community hospital, transferred to a tertiary care facility, and developed multiorgan failure. Nine days after eating the mushrooms, he died. Leftover mushrooms were identified as *A. phalloides* by a mycologist.

In the fifth "group," a 68-year-old man collected mushrooms on a golf course. He had collected mushrooms "hundreds of times" over "many" years in the Philippines, where he had learned about wild mushroom collecting from family members, but this was the first time he had collected them since moving to the United States 9 years previously. He cooked the mushrooms in a soup. He was admitted to a local hospital with an initial diagnosis of gastroenteritis. The history of mushroom ingestion was not elicited until 3 days after admission, and therefore, he never received activated charcoal. Seven days after ingestion, he died.

Discussion

Clinical symptoms and treatment

All 10 poisonings were likely due to ingestion of *A. phalloides,* an amatoxin-containing mushroom. All case-patients had a delayed onset of gastrointestinal symptoms (8–16 hours), which is typical for *A. phalloides.*[10] Mushroom poisonings with delayed onsets—6 hours or more after ingestion—tend to be life-threatening poisonings, while poisonings with onsets less than 2 hours after ingestion are rarely lethal.[2,11] Co-ingested mushrooms that cause symptoms soon after ingestion, however, may mask the asymptomatic period of a lethal mushroom ingestion.[2,5,7] The first group, the Russian family, probably ate more than one type of mushroom, since *Boletus amygdalinus* would not be expected to produce the hepatoxicity they experienced.

The case-patients in this series exhibited the characteristic progression of cellular damage recognized after ingestion of *A. phalloides.* After vomiting and diarrhea subside, patients clinically improve 24 to 48 hours after ingestion; however, the hepatotoxic and nephrotoxic effects then begin to manifest, as occurred in nine of the patients (Table 1).[5,7] Fulminant hepatic failure, encephalopathy, renal failure, hypofibrinogenemia and coagulopathy, acidosis, hypoglycemia, and gastrointestinal hemorrhage may occur.[7,12]

Fatalities have been correlated with young age (<10 years), short latency from ingestion to onset of gastrointestinal symptoms, and the severity of coagulopathy.[6,13] In our case series, the two patients with the highest PTs died; one of the deaths also occurred in the patient with the shortest latency period (Table 1). Twenty percent of the patients in our series died, consistent with published mortality rates of 9%–30%.[3,10,11,14,15] Multiorgan failure preceded the two deaths in our case series, but, in agreement with published reports, transaminase levels in the first few days did not directly correlate with death.[6,13,16]

The serious toxic effects of *A. phalloides* have been attributed to amanitins, cyclic octapeptides.[6] These amatoxins interrupt protein synthesis and cause cell death.[6,17–20] Because of their high rate of protein synthesis, gastrointestinal and liver cells are particularly susceptible to injury, causing the characteristic signs and symptoms of toxicity.[6,11,19,20] Amatoxins are readily absorbed from the intestine and are transported across the hepatocyte by bile transport carriers.[21] About 60% of the toxin undergoes enterohepatic circulation by biliary excretion,[18] and the circulating serum toxin is eliminated rapidly in the urine.[11,18,19] Thus, early hydration and interruption of the enterohepatic circulation are important in the treatment of *A. phalloides* poisoning.

To optimize care, early diagnosis is essential. Health care providers should always consider mushroom ingestion in the differential diagnosis of patients who present with gastrointestinal symptoms and remember that patients may not attribute their symptoms to wild mushrooms eaten 6 to 24 hours earlier. Mushroom particles should be evacuated from the stomach if the patient is seen within 1 hour of ingestion. Activated charcoal should be given immediately to bind any remaining toxin in the gastrointestinal tract. To interrupt the enterohepatic circulation of the toxin, repeated doses of activated charcoal should be administered; gastroduodenal drainage may also be beneficial. Early and aggressive intravenous fluids/electrolytes to correct and maintain adequate hydration and electrolyte balance are essential, and other supportive care should be given (such as fresh frozen plasma and vitamin K for coagulopathy). Other proposed, but unproven, treatments include high-dose penicillin G, silibinin, cimetidine, and *N*-acetylcysteine.[6,7,13] Although there have been no definitive controlled trials, silibinin and high-dose penicillin G appear to be the most promising.[6,7,11,15,19] Silibinin has not been approved for use in the United States.[6] Hemoperfusion, hemodialysis, and hemofiltration to eliminate amatoxin are of limited value.[19] Liver transplantation is indicated for fulminant hepatic failure. Patients with markedly prolonged PT that is only partially correctable and other findings such as acidosis, hypoglycemia, gastrointestinal hemorrhage, hypofibrinogenemia, and increased ammonia level after a significant increase in liver enzymes should be evaluated for urgent liver transplantation, ideally before progressing to advanced hepatic encephalopathy.[3,12] A liver transplant service and poison control center should be contacted early in the hospital course to guide treatment and to expeditiously identify liver transplant candidates (Table 2).

Seasonality and locations of A. phalloides

All cases described in this series occurred during the peak season for *A. phalloides*, the fall and winter months in California; *A. phalloides* has, however, been found throughout the year.[11] The public should be reminded frequently that eating wild mushrooms can be fatal, and

TABLE 2.—*Recommended Care of Suspected Cases of Poisoning due to A. Phalloides*

Obtain a full history including time of eating the mushrooms, time of onset of symptoms, and number of mushroom species eaten
Submit mushroom remnants to an expert mycologist for identification
Ask about others who may have ingested mushrooms so that they can be promptly evaluated
Immediately administer oral activated charcoal
Hydrate with intravenous fluids to correct dehydration and maintain adequate urine output for elimination of the toxin
Monitor and support all vital functions
Prevent toxin absorption by interrupting the enterohepatic circulation of the toxin with repeated doses of activated charcoal (duodenal drainage with a nasoduodenal tube may also be of benefit)
Manage fluid balance, electrolytes, and blood glucose
Monitor and manage complications due to impaired liver function, renal function, and coagulopathy
Call the local poison control center for further advice on clinical management
Liver transplantation: Call the liver transplant service early in the course of management so that the appropriate patients can be transferred to a tertiary care facility and liver donor candidates can be identified, if necessary
Call the local health department early to facilitate investigations and appropriate public health announcements and warnings

medical care providers should consider *A. phalloides* poisoning throughout the year, particularly during the fall and winter months in the West.

Distinguishing A. phalloides

None of the methods stated by the collectors is adequate to identify edible mushrooms. There is no single test that can be used to determine the edibility of wild mushrooms. As has been stated, "NO RULE IS THE ONLY RULE."[1]

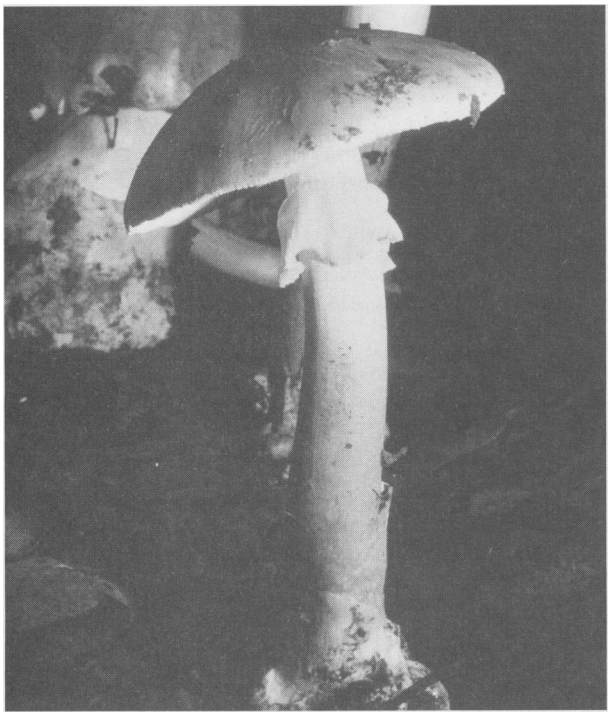

Figure 1.—The classic annulus and volva of an *Amanita phalloides* mushroom. (Photo by Kent R. Olson, MD)

A. phalloides is distinguished by an annulus (or skirt-like ring) around the midportion of the stem, white gills under the cap that are not attached to the stem, and a volva (or cup) at the base of the stem (Fig. 1).[10] Although the cup is an important distinguishing feature, it is easily left behind in the soil if the mushroom is broken off at the stem. The color of *Amanita* species has been described as pure white to moderate olive, olive-gray, greenish yellow, or yellowish brown.[22–24] *A. phalloides* is known to have variable appearances at different times of the year and at different locations, depending on weather, soil, and age of the mushroom.[10,13] Although *A. phalloides* is the most important cause of amatoxin poisoning, other *Amanita* species and *Galerina*, *Lepiota*, *Conocybe*, and *Corinarius* species also contain amatoxin.[6,10] Thus, distinguishing amatoxin-containing mushrooms can be quite difficult. There are edible species of mushrooms that appear similar in appearance to *A. phalloides*; however, because of the difficulty in distinguishing such edible species from *A. phalloides*, any mushrooms that fit the above description should never be ingested.

Immigrants, even if very experienced in their countries of origin, may not be able to distinguish poisonous from edible mushrooms in the United States. Two of our case-patients collected mushrooms for the first time in the United States although they had had significant experience in their native countries.

As illustrated by our case series, knowledge of mushrooms gained from family members or field guides is not sufficient to distinguish *A. phalloides* from edible mushrooms. If wild mushrooms are to be eaten, each specimen should be examined by a competent mycologist; experts may be found at local mycological societies and at university mycology and botany departments. Some may be willing to examine wild mushrooms, but it is impractical to expect that they will provide this service. There is no effective way to render *A. phalloides*

TABLE 3.—*Recommendations for Public Announcements*

Collecting and eating wild mushrooms can be dangerous and even deadly
One of the most deadly mushrooms can be found near populated areas in California
This deadly mushroom has a variable appearance: field guides and simple tests or rules cannot reliably differentiate poisonous from edible mushroom species
Relying on knowledge of family members with many years of experience in mushroom collecting is not adequate to distinguish this deadly mushroom
If wild mushrooms must be eaten, each mushroom should be examined individually by a competent mycologist and deemed edible
If you become ill after ingesting wild mushrooms, seek early medical care, mention the ingestion of wild mushrooms, and bring mushroom remnants for identification

mushrooms safe. Cooking or drying does not detoxify amatoxin, and the mushroom does not have a distinct smell or taste.[3,5,7] Accordingly, the selection of wild mushrooms for consumption should be left to recognized experts.

Awareness of potential dangers of poisonous mushrooms

Despite the fact that all interviewed case-patients knew that poisonous mushrooms existed, seven consciously ate wild mushrooms. Prior media exposure about mushroom poisoning was limited; only one person reported hearing about the dangers of mushroom poisoning in the media that year. Just as there are annual warnings before Thanksgiving about cooking poultry properly, public health announcements to warn the public about the potentially lethal consequences of wild mushrooms should be a routine event when the rains begin every fall (Table 3).

Reporting

Mushroom poisoning is reportable as a foodborne disease in California, and regulations require reporting of suspected cases by the health care provider by fax, telephone, or mail within 1 working day to the local health department. If there are two or more cases or suspected cases from separate households, there is an immediate reporting requirement by telephone.[25] Reporting facilitates public health follow-up, including announcements to the public.

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